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Portal, Mesenteric, and Splenic Vein Thromboses After Splenectomy in a Patient With Chronic Myeloid Leukemia Variant With Thrombocythemic Onset

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Portal, mesenteric, or splenic vein thrombosis is a very uncommon complication with significant mortality in the patients undergoing splenectomy for hematologic disorders. We report a 49-year-old woman who developed portal, superior mesenteric, and splenic vein thromboses after splenectomy. Four years before the event, she presented with a marked thrombocytosis and was diagnosed to have chronic myeloid leukemia variant with thrombocythemic onset as evidence by Philadelphia (Ph^1) chromosome and a b3a2 BCR/ABL transcript. Six weeks after splenectomy, she developed severe epigastric pain. The diagnosis of thromboses of portal, mesenteric, and splenic veins was made by computed tomography scan and Doppler sonogram. She was successfully treated with antegrade intraarterial urokinase therapy via superior mesenteric artery and long-term anticoagulant therapies. To our knowledge, our patient is the first case of portal, mesenteric, and splenic vein thromboses after splenectomy in a patient with CML variant with thrombocythemic onset successfully treated with antegrade intraarterial thrombolytic therapy followed by anticoagulant therapies. Am. J. Hematol. 61:212–215, 1999.

Key words: chronic myeloid leukemia; thrombolysis; thrombosis; essential thrombocythemia; splenectomy

INTRODUCTION

Portal, mesenteric, or splenic vein thromboses after splenectomy for hematologic disorders infrequently occurs with an incidence of 0.2–6% [1] and is associated with a varying mortality between 0% and 75% [2]. Once this diagnosis is established, urgent treatment with thrombolytic agents followed by long-term anticoagulation is needed [3]. Some patients with Ph^1-positive chronic myeloid leukemia (CML) may present with thrombocytosis as the only feature. It has been suggested that this should be called CML variant with thrombocythemic onset [4,5]. We report the first case of portal, mesenteric, and splenic vein thromboses after splenectomy in a patient diagnosed as Ph^1-positive CML variant with thrombocythemic onset where antegrade intraarterial infusion of thrombolytic agent followed by anticoagulant therapies was successfully treated.

CASE REPORT

A 49-year-old woman was admitted, complaining of left upper quadrant pain for 2 months. Four years before the admission, she presented with a white cell of 11,200/μl hemoglobin of 7.0 g/dl, platelet of 911,000/μl, and a normal leukocyte alkaline phosphatase (LAP) score, and examination did not reveal splenomegaly. She presented clinically with ET. However, the final dignosis was CML variant with thrombocythemic onset on the basis of bone marrow (BM) cytogenetic study of t(9;22) (q34;q11) [20/20 metaphases] and reverse transcription polymerase

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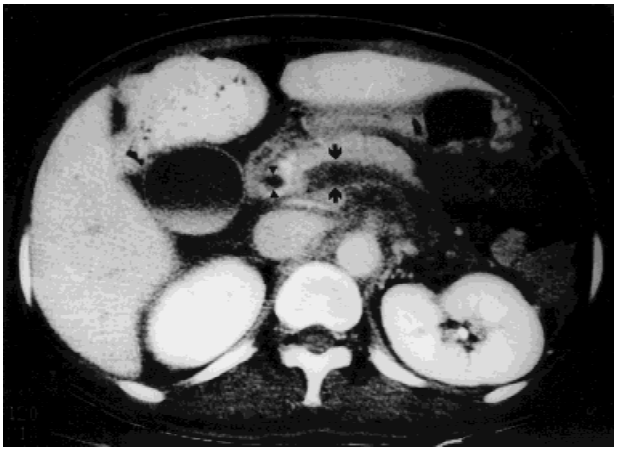

Fig. 1. Abdominal computed tomogram with contrast enhancement shows thrombi in portal (arrowheads) and splenic veins (arrows).

chain reaction (RT-PCR) analysis of b3a2 BCR/ABL mRNA. She was treated with hydroxyurea and intermittent platelet apheresis, and was dependent on red cell transfusion.

At present admission, the blood pressure was 120/80 mmHg, the heart rate was 82/min, the temperature was 37.5°C, and the respiratory rate was 20/min. On examination, she appeared chronically ill and tender splenomegaly was noted. The blood counts were a white cell count 16,400/μl, hemoglobin 10.4 g/dl, and platelet count 206,000/μl. A computed tomography (CT) scan of the abdomen showed huge splenomegaly with a wedge-shaped infarction. She underwent splenectomy and the histologic examination of the splenic tissue showed multifocal infarctions and diffuse infiltration of leukemic cells.

On the third week after splenectomy, she begun to develop mild epigastric pain and showed leukocytosis (33,000/μl) and thrombocytosis (1,225,000/μl). She received hydroxyurea and supportive care. This epigastric pain rapidly became worse, simulating acute pancreatitis, on the sixth hospital week. The blood count showed a white blood cell of 1,700/μl, hemoglobin of 10.2 g/μl, and platelet of 26,000/μl, which indicated bone marrow suppression due to hydroxyurea. However, the serum amylase and lipase were not elevated. The second CT scan and the Doppler sonogram of the abdomen revealed thrombi in the portal, superior mesenteric, and splenic veins with resultant interruption of flow (Fig. 1 and 2A). There was no evidence of small bowel infarction. Other laboratory tests showed no evidence of blood coagulation disorders: antithrombin III 25.5 mg/dl (range, 22–39), protein C 0.14 mg/dl (range, 0.18–0.39), protein S 1.21 mg/dl (range, 1.3–2.1), and negative antiphospholipid antibodies.

An antegrade intra-arterial lytic therapy with urokinase via the superior mesenteric artery was given along with aggressive platelet support, because of severe thrombocytopenia contraindicating systemic thrombolytic therapy or heparinization (Fig. 3A). Bolus injection of 250,000 U urokinase into the superior mesenteric artery was given, followed by a continuous infusion at 100,000 U/hr for 5 days. Angiography and CT scan were repeated daily. On the second day of urokinase infusion, she showed a significant relief of abdominal pain and some antegrade flow into the superior mesenteric vein on angiogram. On the fifth day, slight patency was found in the portal vein, but Doppler sonogram revealed residual thrombus in the portal and splenic vein (Fig. 3B).

Thereafter, she received combined systemic heparin-warfarin therapy for 5 days, and was maintained on oral warfarin and 100 mg/day of aspirin. The prothrombin time was maintained at an International Normalized Ratio (INR) of 2 to 3. Three months later, Doppler sonogram showed near complete resolution of thrombi in the portal vein and superior mesenteric veins with flow signals (Fig. 2B). Presently, she remains well on warfarin, aspirin, and hydroxyurea therapy.

DISCUSSION

Both CML and ET are chronic myeloproliferative disorders. The updated diagnostic criteria for ET established by the Polycythemia Vera Study Group (PVSG) include an absence of Ph^1 chromosome and BCR/ABL hybrid gene [6]. However, some patients present clinically with ET, but have Ph^1 chromosome and/or BCR/ABL rearrangement. Some investigators [7,8] have described these subgroups as the Ph^1-positive form of ET. Recently, these subgroups are considered the Ph^1-positive CML variant with thrombocythemic onset because of progression to either the accelerated or blastic phase [4,5].

Several cases of portal, mesenteric, or splenic vein thrombosis, since the first reported by Delatour et al. [9], have been reported in patients undergoing splenectomy for hematologic disorders such as myeloproliferative disorder, hemolytic anemia, idiopathic thrombocytopenic purpura, hereditary spherocytosis, and idiopathic portal vein thrombosis [3]. Although the pathogenesis of this phenomenon is still unexplained, two pathogenetic factors such as hypercoagulable state and blood stasis can be speculated [3]. The time interval between splenectomy and thrombosis varies from 6 days to 3 years [10]. Thrombotic complication in myeloproliferative disorder is not related to the platelet counts, but to the platelet function abnormalities [11]. Also, there is no parameter for predicting thrombotic manifestation. The diagnosis of portal or mesenteric vein thrombosis is based on the clinical suspicion, confirmed with an imaging procedure, such as Doppler ultrasonography, contrast-enhanced CT

Fig. 2. (A) Doppler sonogram shows compact thrombi in the portal (arrows) without Doppler signal. (B) After 3 months, thrombi in the portal vein shows near complete resolution with good flow signals (arrows).

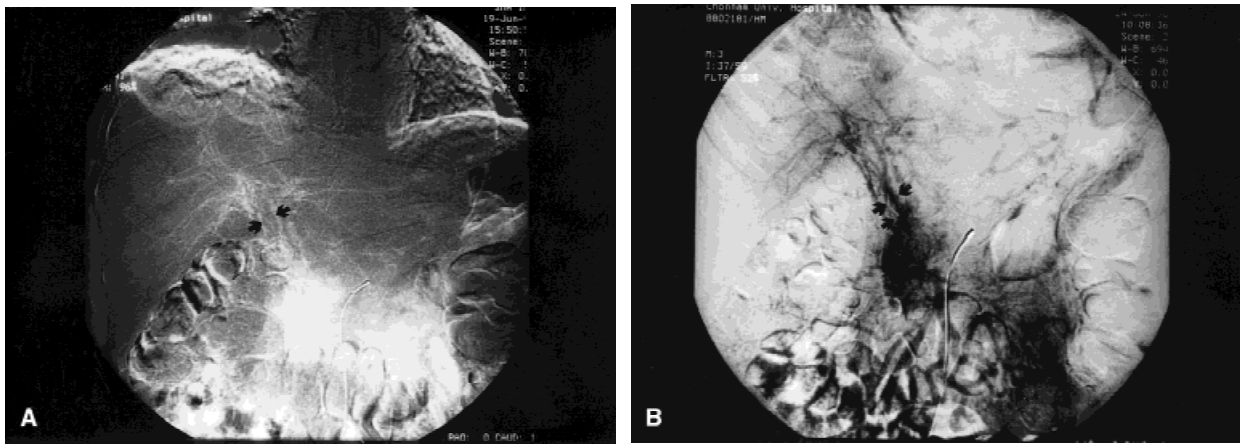

Fig. 3. (A) Initial mesoportogram reveals filling defect (arrows) in main portal vein with poorly development of collateral vessels. (B) Follow-up mesoportogram at 5 days of urokinase infusion shows slight disappearance of portal vein thrombosis (arrows).

scan, magnetic resonance imaging angiography, or, rarely, arteriography [3].

Our patient initially presented with ET due to marked thrombocytosis, absence of splenomegaly, and normal LAP score. However, on the basis of the karyotypic finding of Ph^1 chromosome and the RT-PCR analysis of b3a2 BCR/ABL transcript, the present case was diagnosed as Ph^1-positive CML variant with thrombocythemic onset [4]. This patient developed thromboses in the portal, splenic, and superior mesenteric veins after splenectomy. Thrombolytic therapy or systemic heparinization was contraindicated due to severe thrombocytopenia. Thus, the antegrade infusion of thrombolytic therapy via superior mesenteric artery was attempted, and the present patient showed a marked improvement of clinical symptoms and nearly complete resolution of thrombi.

Gertsch et al. [2] reported a varying mortality rate depending on the extent of thrombosis: the thrombosis of superior mesenteric and splenic vein is 76% and superior mesenteric vein alone is 18%. Thus, once the diagnosis of thrombosis is established, urgent treatment with thrombolytic agents followed by long-term anticoagulation is essential to be lifesaving [12,13]. Antegrade intraarterial infusion of thrombolytic agent is an effective and safe approach without life-threatening complications or technical difficulties [12]. Patients with evidence of bowel infarction should undergo laparotomy and bowel resection. In addition, prophylactic therapy with anticoagulant or antiplatelet agents is needed.

In conclusion, the present report suggests that portal vein and splenic vein thrombosis should be considered in patients with abdominal pain after splenectomy for myeloproliferative disorders, and the antegrade intra-arterial infusion of thrombolytic therapy followed by anticoagulant therapies for these patients may be a simple and effective approach.

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